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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,728	10/25/2001	Roberto Fagnani	71726 / 6776	3521

7590 08/04/2009

Fitch, Even, Tabin & Flannery
Suite 1600
120 S. LaSalle St.
Chicago, IL 60603

EXAMINER	
LUNDGREN, JEFFREY S	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
08/04/2009	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ROBERTO FAGNANI, SOONKAP HAHN, XIAOFAN DONG, TONY PIRCHER, SANDRA MATSUMOTO, and PAVEL TSINBERG

Appeal 2008-006232
Application 10/054,728
Technology Center 1600

Decided: August 4, 2009

Before LORA M. GREEN, FRANCISCO C. PRATS, and JEFFREY N. FREDMAN, *Administrative Patent Judges.*

GREEN, *Administrative Patent Judge.*

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 43, and 46. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

The claims are directed to a biochip. Claims 1 is representative of the claims on appeal, and reads as follows:

1. A biochip comprising:
   a) a solid substrate having a flat top surface;
   b) a plurality of optically clear, individual, three-dimensional hydrogel cells at least 20 μm thick attached to the flat surface of the substrate at discrete locations to form an array of discrete individual three-dimensional cells protruding from said otherwise flat top surface, which hydrogel cells are formed from an isocyanate-functional prepolymer with urethane linkages; and
   c) a different binding entity immobilized within or upon various of said hydrogel cells by covalent linkage of said binding entity or an intermediate agent with reactive isocyanate groups of said hydrogel, which entity is effective to selectively hybridize to or sequester a target molecule.

The Examiner relies on the following evidence:

Braatz	US 5,169,720	Dec. 8, 1992
Sundberg	US 5,624,711	Apr. 29, 1997
Wagner	US 6,406,921 B1	Jun. 18, 2002

The following grounds of rejection are before us for review:

I) Claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 43, and 46 stand rejected under 35 U.S.C. § 112, first paragraph, as containing new matter;

II) Claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, and 46 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Sundberg and Braatz; and

III) Claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 41-43, and 46 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Wagner, Braatz, and Sundberg.

We reverse.

ISSUE (New Matter)

The Examiner finds that the limitation of "flat top" is new matter, and thus rejects claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 43, and 46 under 35 U.S.C. § 112, first paragraph.

Appellants contend that the objected to limitation is supported as the disclosure as filed.

Thus, the issue on appeal is: Have Appellants demonstrated that the Examiner erred in finding that the limitation "flat top" constitutes new matter?

FINDINGS OF FACT

FF1 The Specification teaches that the "biochip substrate may consist of a variety of materials and formats which are conductive to automated handling during a binding assay and later detection of target molecules binding to the individual cells." (Spec.[1] 20-21.)

FF2 The Specification teaches that "[a]lthough solid flat plates, e.g., glass slides, are suitable, plates that have depressions or wells formed therein to hold individual cells may be used." (*Id.* at 21.)

[1] All references to the Specification are to the substitute Specification dated November 12, 2003.

FF3 The Examiner rejects claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 43, and 46 stand rejected under 35 U.S.C. § 112, first paragraph, as containing new matter (Ans. 3).

FF4 The Examiner finds that "the claims have the limitation 'flat top' which is neither supported literally in the Specification, or adequately by way of example." (*Id.*)

PRINCIPLES OF LAW

The disclosure as originally filed need not provide "*in haec verba* support for the claimed subject matter at issue," rather, the disclosure should convey to one skilled in the art that the inventor has had possession of the invention at the time of filing. *Purdue Pharma L.P. v. Faulding Pharmaceutical Co.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000) (citations omitted).

ANALYSIS

Appellants argue that the Specification teaches "that the substrates may be solid flat plates, e.g. glass slides," and thus the disclosure as filed supports the limitation that the biochip comprises "a solid substrate having a flat top surface." As we agree with Appellants that the disclosure as filed demonstrates descriptive support for the above limitation, we reverse the Examiner.

CONCLUSION OF LAW

We find that Appellants have demonstrated that the Examiner erred in finding that the limitation "flat top" constitutes new matter.

We thus reverse the rejection of claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 43, and 46 under 35 U.S.C. § 112, first paragraph.

ISSUE (Obviousness)

The Examiner concludes that claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, and 46 are rendered obvious by the combination of Sunberg and Braatz; and that claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 41-43, and 46 are rendered obvious by the combination of Wagner, Braatz, and Sunberg.

Appellants contend that the Examiner has engaged in improper hindsight in combining the references.

Thus, the issue on appeal is: Have Appellants demonstrated that the Examiner erred by engaging in hindsight in combining the references to arrive at the claimed invention?

FINDINGS OF FACT

FF5 The Examiner rejects claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, and 46 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Sunberg and Braatz (Ans. 3).

FF6 The Examiner cites Sundberg for teaching "a polymer covered support (refers to instant claimed solid substrate) and an array of ligands such as peptides (refers to instant claimed binding entity . . .)." (*Id.*)

FF7 The Examiner finds that Sundberg teaches that the polymer coating provides "a porous three-dimensional matrix functionalized with reactive groups, and greater solvent compatibility and flexibility of the reaction site for attachment." (*Id.* at 3-4.)

FF8 The Examiner further finds that Sundberg teaches that the "polymer coating includes polyurethanes or polyethylene glycol and isocyanate functional group for the attachment of the ligands (refers to instant claimed isocyanate-functional polymer/urethane linkages . . .) (see e.g. col. 5, lines 25-35; col. 11, lines 59-62)." (*Id.* at 4.)

FF9 Sundberg "provides a variety of derivatized supports and methods for their preparation, which are useful in the preparation of peptides, oligonucleotides or other small organic molecules." (Sundberg, col. 1, ll. 64-67.)

FF10 Sundberg teaches that the derivatized support may have an altered surface, such as being coated by a polymer (*id.* at col. 2, ll. 5-7).

FF11 Specifically, Sundberg teaches that the support may be derivatized with a trialkylsilane having a reactive site, such as a isothiocyanate, for the attachment of suitable linking groups, whereas in another aspect, the support may be coated with a stabilized polymer for use in solid-phase synthesis (*id.* at col. 2, ll. 15-38).

FF12 Sundberg teaches that the polymers used for coating the solid support "include . . . polyurethanes," and are "typically repeats of a single monomers [sic] which is crosslinked with a second molecule to provide structural integrity to the polymer." (*Id.* at col. 5, ll. 25-35.)

FF13 Sundberg teaches that the selection of an appropriate polymer includes considering its compatibility with the oligomer synthesis method, and thus must be stable in the presence of solvents and activating reagents used, but exhibit low specific binding of receptors (*id.* at col. 14, ll. 31-48).

FF14 Sundberg also teaches that the polymer may be selected based on the functional group that serves as the synthesis initiation site, and typically will have primary amine, carboxyl, or hydroxyl functional groups (*id.* at col. 14, ll. 49-54).

FF15 The Examiner notes that the "supports . . . differ from the presently claimed invention [by] not reciting a polymer comprising an isocyanate-capped polyurethane prepolymer." (Ans. 4.)

FF16 The Examiner finds that Braatz teaches polymer-coated devices, wherein the "polymer coatings comprise isocyanate end-capped prepolymer oxyethylene based diols or glycols." (*Id.*)

FF17 The Examiner finds further that Braatz teaches that the "polymer hydrogels have many applications," such as coating of "*assay plates, supports, or membranes*." (*Id.* at 14.)

FF18 Braatz teaches polyurea-urethane polymer coatings that have "highly desirable properties which make them particularly well suited for use in the growing field of biomedical applications." (Braatz, col. 2, ll. 46-49.)

FF19 Braatz teaches that an object of the invention is thus "to provide a class of hydrated polymers for which ease of preparation and handling is combined with desirable properties permitting a wide range of end uses." (*Id.* at col. 2, ll. 65-68.) In particular, the coatings are resistant to non-specific protein absorption (*id.* at col. 10, ll. 28-29).

FF20 Braatz teaches that the coatings made be used on tubing for use in medical devices, such as kidney dialysis and hemoperfusion devices, but other devices may be coated, such as "assay plates, supports or membranes, glassware, cell culture or bioreactor devices or assemblies, tubing for blood transfer, blood cell storage bags, filters, pharmaceutical manufacturing and packaging, protein isolation, preparation and purification devices or systems, etc." (*Id.* at col. 11, l. 48-col. 12, l. 5.)

FF21 Braatz does not teach or suggest covalent coupling to the coated surface, such as covalent coupling of proteins to the surface through free isocyanate groups or through a linker.

FF22 The Examiner concludes that it would have been obvious to use isocyanate-capped polyurethane prepolymer with the gel matrix of Sundberg

> for the advantage of providing a class of hydrated polymers for which ease of preparation and handling is combined with desirable properties (e.g., reduced protein adsorption/biofouling, as explained by Braatz) permitting a wide range of end uses (Braatz: col. 2, lines 65-68) since both Sundberg and Braatz disclose a support comprises coated polymers with hydroxyl functional group such as polyethylene glycol (Sundberg: col. 15, lines 21-25; Braatz: col. 4, lines 16-22). In addition, Sundberg discloses that surfaces can be designed and prepared for optimum properties in a particular assay (Sundberg: col. 14, lines 2-6) and as a result the type of polymer use would be a choice of experimental design and is considered within the purview of the cited prior art. Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Sundberg et al. and Braatz et al. because Braatz et al. disclosed by example the success of coating surfaces with a polymer comprising an isocyanate-capped polyurethane prepolymer (Braatz: col. 19, line 47 thru col. 20, line54).

(Ans. 5.)

FF23 The Examiner rejects claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, 41-43, and 46 under 35 U.S.C. § 103(a) as being obvious over the combination of Wagner, Braatz, and Sunberg (Ans. 5).

FF24 The Examiner finds that Wagner teaches "an array of proteins comprising a plurality of patches in discrete, known regions on a substrate, where the protein has different, known sequence is immobilized on each patch and the method of making an array of protein capture agents." (*Id.* at 6.)

FF25 The Examiner finds that the array of Wagner

> comprises of a monolayer (refers to instant claimed hydrogel) on the surface of the substrate and the proteins are immobilized on the monolayer (see e.g. col. 8, lines 10-17; col. 11, lines 15-28 and 39-53). The monolayer comprises the formula of X-R-Y wherein X is the functional group that binds to the surface of the substrate, R is a hydrocarbon chain with the hetero groups such as -(OCH2CH2)n- with n =1-20, and Y is the functional group that binds to the protein such as isocyanate (see e.g. col. 8, lines 10-17; col. 10, lines 10-26; col. 1 1, lines 15-28 and 39-53).

(*Id.*)

FF26 Wagner teaches a protein array (Wagner col. 3, ll. 16-22), in which a protein may be immobilized on a portion of the substrate through a monolayer (*id.* at col. 4, ll. 21-36).

FF27 Wagner teaches that the monolayer comprises molecules of the formula X-R-Y, where R is a spacer, X is a functional group that binds R to the surface, and Y is a functional group for binding the protein onto the monolayer (*id.* at col. 4, ll. 29-36). The monolayer of Braatz is thus a single-

molecule thick layer of molecules attached to the surface of the biochip (*id.* at col. 5, ll. 56-57).

FF28 Wagner does teach that a hydrogel may be used as a functional moiety to immobilize a protein onto the monolayer, and may be used to covalently or noncovalently attach the protein to the surface (*id.* at col. 5, ll. 36-45).

FF29 The Examiner notes that the "support of Wagner differs from the presently claimed invention by failing to [disclose] a polymer comprising an isocyanate-capped polyurethane prepolymer." (Ans. 6.)

FF30 The Examiner relies on Braatz as set forth above (Ans. 6-7).

FF31 The Examiner concludes that it would have been obvious to the ordinary artisan

> to provide a polymer comprising an isocyanate-capped polyurethane prepolymer as taught by Braatz . . . . for the advantage of providing a class of hydrated polymers for which ease of preparation and handling is combined with desirable properties permitting a wide range of end uses (Braatz: col. 2, lines 65-68) since both Wagner and Braatz disclose a support comprises coated polymers with hydroxyl functional group such as polyethylene glycol (Wagner: col. 12, lines 31-38; Braatz: col. 4, lines 16-22). In addition, Wagner disclose that there are many possible design choices with regard to the type of coating on the substrate (Wagner: col. 8, lines 34-38) and as a result the type of polymer use would be a choice of experimental design and is considered within the purview of the cited prior art (see Sundberg).

(*Id.* at 7.)

PRINCIPLES OF LAW

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966).

While the analysis under 35 U.S.C. § 103 allows flexibility in determining whether a claimed invention would have been obvious, *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007), it still requires showing that "there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *Id.* "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently known in the prior art." (*Id.*) Therefore, "[w]e must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention." *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008).

ANALYSIS

Appellants argue that the Examiner engaged in impermissible hindsight in substituting the polymer of Braatz for the polymer coating of Sundberg (App. Br. 11-12). Appellants assert that Sundberg is drawn to the *in situ* building of a microarray by synthesizing oligomers at predetermined locations, and thus requires "a polymeric resin having synthesis initiation

sites which will serve as the base upon which the solid-phase synthesis can be initiated." (*Id.* at 12.) Braatz, Appellants assert, teaches "the creation of a polyurea-urethane polymer that is protein non-absorptive," and thus "is clearly not a coating that one would consider using a base for synthesizing peptides or proteins *in situ* to create an array, nor is it one that would be effective." (*Id.*)

According to Appellants, Braatz teaches elimination of any residual surface reactive isocyanate groups, creating a coated substrate that would not be useful in the Sundberg procedure, which requires a polymeric resin that has reactive groups required for the initiation of oligomer synthesis (*id.*).

The Examiner responds that "Appellants' arguments fail to consider the art as a whole from the perspective of the person of ordinary skill." (Ans. 14.) According to the Examiner, Sundberg teaches the use of isocyanate groups for attachment to the derivatized surface, and thus "one of ordinary skill in the art would have recognized that isocyanate prepolymers/hydrogel strategy of Braatz, in view of the isocyanate groups of Sundberg, provide the means for linking biological components, and attachment for various linking moieties." (*Id.* at 15.) The Examiner responds further that the claims read "on 'an intermediate agent' that reacts with the isocyanate groups in the prepolymer reagent, such as the linkers in Sunberg." (*Id.*)

We conclude that Appellants have the better position. Sundberg is drawn to *in situ* synthesis of oligomers, such as peptides, nucleotides, etc., and Sundberg sets forth a list of requirements for any polymeric coating. Conversely, Braatz is drawn to a polymeric coating that resists protein

absorption. Braatz does not teach or suggest covalent attachment of any molecule to the polymer, but instead touts its resistance to non-specific protein absorption. Thus, we agree with Appellants that while the Examiner has found the individual elements of the claimed biochip, the ordinary artisan would not have looked to the polymeric coating of Braatz as a substrate for oligomeric synthesis reactions.

The Examiner asserts that Sundberg teaches the use of isocyanate groups for attachment to the derivatized surface, but that teaching is in the context of adding a molecule, such as a linker, etc., to the surface of the substrate, such as a glass slide, and not to the use of the group as the attachment site for the initiation of oligomer synthesis. In fact, Sundberg teaches that the polymeric coating will typically have primary amine, carboxyl, or hydroxyl functional groups that serve as the synthesis initiation site.

As to the combination of Wagner and Braatz, Appellants again argue that the Examiner has engaged in impermissible hindsight (App. Br. 16). According to Appellants, "Braatz does not use an isocyanate-functional hydrogel to which protein or other binding entities can be attached by covalent linkage," as it teaches a polymer coating that is protein non-absorptive (*id.*).

The Examiner responds that "Wagner is an appropriate reference that clearly illustrates that bioarrays for assay purposes based on polyethylene chemistries, and having isocyanate functional groups may utilize a chemical group such as nitrilotriacetic acid as an intermediate en route to preparing a

gel-based substrate such as Sundberg, made from an isocyanate-functional prepolymer with urethane linkages as shown by Braatz." (Ans. 17.)

Again, we find that Appellants have the better position. First, we disagree that Wagner would characterize the monolayer as a hydrogel, as found by the Examiner. The monolayer of Wagner has the formula X-R-Y wherein X is the functional group that binds to the surface of the substrate, R is a hydrocarbon chain with the hetero groups such as -(OCH2CH2)n- with n =1-20, and Y is the functional group that binds to the protein such as isocyanate. Wagner then goes on to teach that a hydrogel may be used as a functional moiety to immobilize a protein onto the monolayer, thus distinguishing the monolayer from the hydrogel.

Moreover, we cannot find a reason as to why the ordinary artisan would substitute the polymeric coating of Braatz for the monolayer of Wagner as suggested by the Examiner. The monolayer has two different functional groups, wherein one functional group is used to covalently attach to the substrate, and the second functional group is used to covalently attach a molecule, such as a protein to the monolayer. While Braatz teaches the use of isocyanate groups in the formation of the disclosed polymer coating, Braatz does not teach that after the polymerization the groups are still available for covalent attachment of proteins to the coating.

CONCLUSIONS OF LAW

We conclude that Appellants have demonstrated that the Examiner erred by engaging in hindsight in combining the references to arrive at the claimed invention.

We are thus compelled to reverse the rejection of claims 1, 3, 5-7, 9, 10, 17, 18, 31-35, and 46 under 35 U.S.C. § 103(a) as being obvious over the combination of Sundberg and Braatz; as well as the rejection of claims 1, 3, 5-7, 9, 10, 17-18, 31-35, 41-43, and 46 under 35 U.S.C. § 103(a) as being obvious over the combination of Wagner, Braatz, and Sundberg.

REVERSED

Ssc:

Fitch, Even, Tabin & Flannery
Suite 1600
120 S. LaSalle Street
Chicago, IL 60603